

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Serial Number:

Application Filed:

Applicant(s): KREAM, Richard M.

Title: Method For Inhibiting Opioid Tolerance With Chimeric Hybrid Analgesics

Art Unit:

Examiner:

INFORMATION DISCLOSURE STATEMENT

October 10, 2003

Commissioner of Patents
United States Patent and Trademark Office
Washington, DC 20231

Sir:

Pursuant to Rule 98(d), the references listed on the attached Forms SB/08 are not enclosed since these were supplied in the parent case, Ser. No. 10/134,187.

Respectfully yours,



Richard M. Kream, Ph.D.
% Chimeracom, LLC
Wall Street Plaza, 23rd Floor
New York, NY 10005-1875
Tel: 631-549-2064
Fax: 212-344-4294

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>		Complete if Known <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%;">Application Number</td> <td>10/134,187</td> </tr> <tr> <td>Filing Date</td> <td>04/26/2002</td> </tr> <tr> <td>First Named Inventor</td> <td>KREAM, RICHARD M.</td> </tr> <tr> <td>Art Unit</td> <td>1614</td> </tr> <tr> <td>Examiner Name</td> <td></td> </tr> <tr> <td>Attorney Docket Number</td> <td></td> </tr> </table>		Application Number	10/134,187	Filing Date	04/26/2002	First Named Inventor	KREAM, RICHARD M.	Art Unit	1614	Examiner Name		Attorney Docket Number	
Application Number	10/134,187														
Filing Date	04/26/2002														
First Named Inventor	KREAM, RICHARD M.														
Art Unit	1614														
Examiner Name															
Attorney Docket Number															
Sheet		of													

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code ² (if known)			
		US- 5,891,842 (B1)	04/06/99	Kream, Richard	
		US- 6,310,072 (B1)	10/30/01	Smith, Marge, et al	
		US- 6,063,758 (B1)	05/16/00	Lappi, Douglas, et al	
		US- 09/428,692	Unpub.	Carr, Daniel, et al	
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ - Number ⁴ - Kind Code ⁵ (if known)				
		PCT WO 01/30371 (A@) 11060598	05/03/01 08/15/97	Carr, Daniel, et al. Matsumura		

Examiner Signature	Date Considered
-----------------------	--------------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Application Number	
		Filing Date	
		First Named Inventor	
		Group Art Unit	
		Examiner Name	
		Attorney Docket Number	
Sheet		of	

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
		REULER, et al., <i>The Chronic Pain Syndrome: Misconceptions & Management</i> , ANN INTERN MED. 93:588-596 (1980)	
		SRIWATANKUL, et al, <i>Analysis of Narcotic Analgesic usage in the Treatment of Postoperative Pain</i> , JAMA 250:926-929 (1983)	
		SCHECHTER, <i>Pain & Pain Control in Children</i> , CURRENT PROBLEMS IN PEDIATRICS 15 (1985)	
		GOODMAN & GILMAN, <i>The Pharmacological Basis of Therapeutics</i> 511 (7 th ed. 1985)	
		FORAN, et al, <i>A Substance P-opioid chimeric peptide as a unique nontolerance-forming analgesic</i> , 97 PNAS 13:7521-26 (2001)	
		EGELTON, et al, <i>Transport of Opioid Peptides into the Central Nervous System</i> , J PHARM SCI 1998, 87(11):1433-39	
		BORCHARD, <i>Optimizing oral absorption of peptides using prodrug strategies</i> , J CONTROL RELEASE 1999; 62(1-2):231-38	
		STAIN-TEXIER, <i>Elevated concentrations of morphine 6-beta-D-glucuronide in brain extracellular fluid despite low blood-brain barrier permeability</i> , BR J PHARMACOL 1999; 128(4):917-24	
		MERRIFIELD, <i>Solid Phase Synthesis</i> , SCIENCE 232: 241-47 (1986)	
		BARANY, et al, <i>Solid-phase peptide synthesis; a silver anniversary report</i> , INT'L J PEPTIDE PROTEIN RES 30:705-39 (1987)	
		KENT, <i>Chemical Synthesis of Peptides and Proteins</i> , ANN REV BIOCHEM 57:857-989 (1988)	

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Application Number	10/134,187
		Filing Date	04/26/2002
		First Named Inventor	KREAM, RICHARD M.
		Group Art Unit	1614
		Examiner Name	
		Attorney Docket Number	
Sheet		of	

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
		KAISER, et al, <i>Peptide & Protein Synthesis by Segment Synthesis-Condensation</i> , SCIENCE 243:187-98 (1989)	
		KREAM, <i>Substance P markedly potentiates the antinociceptive effects of morphine sulphate administered at the spinal level</i> , 90 PNAS 5564-68 (1993)	
		MASCZYNSKA, et al, <i>Alternative forms of interaction of substance P and opioids innocicpetive transmission</i> , LTRS PEPTIDE SCI 298, 5:395-98 (1998)	
		MASCZYNSKA, et al, <i>Dual Functional Interactions of Substance P Opioids in Nociceptive Transmission</i> , ANALGESIA 3:259-68 (1998)	
		WATSON, et al, <i>Tissue Selectivity of Substance P Alkyl Esters Suggesting Multiple Receptors</i> , EURO J PHARMACOL 87:77-84 (1983)	
		SIZHENG, et al, <i>Opioid and neurokinin activities of substance P fragments and their analogs</i> , EURO J PHARMACOL 193:209-15 (1991)	
		LIPKOWSKI, et al, <i>An Approach to the Self Regulatory Mechanism of Substance P Actions</i> , 33 LIFE SCIENCES 141-44 (1983)	
		FORAN, et al, <i>Inhibition of Morphine tolerance Development by a Substance P-Opioid Peptide Chimera</i> , J PHARMACOL & EX THERA 295:3:1142-48 (2000)	
		LIPKOWSKI, et al, <i>Opioid Peptide Analogues: Reconsideration as a Potentially New Generation of Analgesics</i> , POLISH J-CHEM, 68:907-12 (1994)	
		MISTEREK, et al, <i>Spinal Co-Administration of Peptide Substnace P Antagonist Increases Antinociceptive Effect of the Opioid Peptide Biphalin</i> , LIFE SCIENCES, 14:939-44 (1994)	
		FORAN, et al, <i>Chimeric Peptide for the Treatment of Acute & Chronic Pain</i> , ANESTHESIOLOGY 91:3A:A944 (1999)	

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

control number.			
Substitute for form 1449B/PTO		Compleat if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>		Application Number	10/134,187
		Filing Date	04/26/2002
		First Named Inventor	KREAM, RICHARD M.
		Group Art Unit	1614
		Examiner Name	
Sheet		of	Attorney Docket Number

[illegible]

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.**

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number 10/134, 187

Filing Date 04/26/2002

First Named Inventor KREAM, RICHARD M.

Art Unit 1614

Examiner Name

Attorney Docket Number

Sheet

1

of

1

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		LIPKOWSKI, ET AL, Neuropeptides: Peptide and Nonpeptide Analogs, PEPTIDES: SYNTHESIS, STRUCTURES AND APPLICATIONS. 1995, PP 287-320. ACADEMIC PRESS.	

Examiner
Signature

Date

Considered

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Washington, DC 20231.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.